

AMENDMENTS TO THE CLAIMS

The following listing of claims replaces all prior versions of claims in the application:

1. (Currently amended) A method for detecting in a nucleic acid sample the presence or absence of a at least two variant nucleotides associated with thrombosis, the method comprising the steps of:

a) amplifying from the sample regions of DNA that include at least two selected nucleotide positions for which variants are known to be associated with thrombosis, to form amplified DNA products;

b) hybridizing at least two of the polynucleotide primers of claim 16 as tagged allele specific extension primers to a complementary target sequence in the amplified DNA products, wherein each tagged allele specific extension primer has a 3'-end hybridizing portion capable of hybridizing to the corresponding amplified DNA, and wherein the 3' end hybridizing portions of the at least two tagged allele specific extension primers each comprise a sequence selected from the group consisting of bases from position 25 to the 3' terminal nucleotide of SEQ ID NO: 1 to SEQ ID NO: 12, and a 5'-end tag portion complementary to a corresponding anti-tag sequence, the terminal nucleotide of the 3' end hybridizing portion being either complementary to a suspected variant nucleotide or to the corresponding wild type nucleotide;

c) extending the at least two tagged allele specific extension primers, using labelled nucleotides, if the terminal nucleotide of each 3' end hybridizing portion is a perfect match to the corresponding amplified DNA product; and

d) hybridizing the at least two tagged allele specific extension primers to their corresponding anti-tag sequences and detecting the presence of labelled extension products.

2. (Previously presented) The method of claim 1, wherein the 5'-end tag portions of the at least two tagged allele specific primers each comprise a sequence selected from the group consisting of bases 1 to 24 of SEQ ID NO: 1 to SEQ ID NO: 12 and wherein the sequence of each 5'-end tag portion is different from each other 5'-end tag portion.

3. (Previously presented) The method of claim 1 wherein the anti-tag sequence is coupled to a solid support.
4. (Previously presented) The method of claim 3 wherein the solid support is selected from the group consisting of beads, spectrally coded beads, and a chip based microarray.
5. (Previously presented) The method of claim 1 wherein the step of amplifying is conducted by PCR using a set of PCR amplification primers, said set comprising at least two pairs of PCR primers selected from the group of pairs consisting of:
SEQ ID NO: 13 and SEQ ID NO: 14, SEQ ID NO: 15 and SEQ ID NO: 16, SEQ ID NO: 17 and SEQ ID NO: 18, SEQ ID NO: 19 and SEQ ID NO: 20, SEQ ID NO: 21 and SEQ ID NO: 22, and SEQ ID NO: 23 and SEQ ID NO: 24, wherein the at least two pairs of PCR primers are selected for their ability to amplify regions of DNA that include sequences to which the selected at least two tagged allele-specific extension primers will hybridize.
6. (Currently amended) A method for detecting in a nucleic acid sample the presence or absence of at least two variant nucleotides associated with thrombosis, the method comprising the steps of;
 - a) amplifying from the sample regions of DNA that include at least two selected nucleotide positions for which variants are known to be associated with thrombosis to form amplified DNA products;
 - b) hybridizing the at least two tagged allele specific extension primers of the kit of claim 10 to a complementary target sequence in the amplified DNA products, ~~wherein the at least two tagged allele specific extension primers are selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 12, each tagged allele specific extension primer having a 3' end hybridizing portion capable of hybridizing to the corresponding amplified DNA, and a 5' end tag portion complementary to a corresponding anti tag sequence, the terminal nucleotide of the 3' end hybridizing portion being either complementary to a suspected variant nucleotide or to the corresponding wild type nucleotide;~~

c) extending the at least two tagged allele specific extension primers, using labelled nucleotides, if the terminal nucleotide of each 3' end hybridizing portion is a perfect match to the corresponding amplified DNA product; and

d) hybridizing the at least two tagged allele specific extension primers to their corresponding anti-tag sequences and detecting the presence of labelled extension products,

7. (Previously presented) The method of claim 6 wherein the anti-tag sequence is coupled to a solid support.

8. (Previously presented) The method of claim 7 wherein the solid support is selected from the group consisting of beads, spectrally coded beads, and a chip based microarray.

9. (Previously presented) The method of claim 6 wherein the step of amplifying is conducted by PCR using a set of PCR amplification primers, said set comprising at least two pairs of PCR primers selected from the group of pairs consisting of:
SEQ ID NO: 13 and SEQ ID NO: 14, SEQ ID NO: 15 and SEQ ID NO: 16, SEQ ID NO: 17 and SEQ ID NO: 18, SEQ ID NO: 19 and SEQ ID NO: 20, SEQ ID NO: 21 and SEQ ID NO: 22, and SEQ ID NO: 23 and SEQ ID NO: 24, wherein the at least two pairs of PCR primers are selected for their ability to amplify regions of DNA that include sequences to which the selected at least two tagged allele-specific extension primers will hybridize.

10. (Currently amended) A kit for use in detecting in a nucleic acid sample the presence or absence of a at least two variant nucleotides associated with thrombosis, said kit comprising a set of at least two tagged allele specific extension primers wherein each tagged allele specific extension primer has a 3'-end hybridizing portion including a 3' terminal nucleotide being either complementary to a variant nucleotide known to be associated with thrombosis or to the corresponding wild type nucleotide and a 5'-end tag portion complementary to a corresponding anti-tag sequence, and wherein the nucleotide sequences of the at least two tagged allele-specific extension primers ~~are~~ consist of the sequences selected from the group consisting of SEQ ID NO: 1 to SEQ ID NO: 12.

11. (Previously presented) The kit of claim 10 further comprising a set of PCR amplification primers, said set comprising at least two pairs of PCR primers selected from the group of pairs consisting of:

SEQ ID NO: 13 and SEQ ID NO: 14, SEQ ID NO: 15 and SEQ ID NO: 16, SEQ ID NO: 17 and SEQ ID NO: 18, SEQ ID NO: 19 and SEQ ID NO: 20, SEQ ID NO: 21 and SEQ ID NO: 22, and SEQ ID NO: 23 and SEQ ID NO: 24, wherein the at least two pairs of PCR primers are selected for their ability to amplify regions of DNA that include sequences to which the selected at least two tagged allele-specific extension primers will hybridize.

12. (Previously presented) The kit of claim 10 further comprising a set of anti-tags, each anti-tag having a sequence complementary to nucleotides 1-24 of the selected at least two tagged allele-specific extension primers.

13. (Previously presented) The kit of claim 12 wherein the anti-tags are coupled to a support.

14 -15. (Canceled)

16. (Previously presented) A composition comprising a plurality of polynucleotide primers for use in detecting the presence or absence of variant nucleotides associated with thrombosis, wherein the plurality of primers comprises oligonucleotides having sequences set forth by position 25 to the 3' terminal nucleotide of SEQ ID NOs: 1-12, or the complete complements thereof.

17. (Previously presented) The composition of claim 16 wherein the plurality of primers consists of oligonucleotides having sequences set forth by SEQ ID NOs: 1-12 or the complete complements thereof.

18. (Previously presented) A combination comprising the composition of claim 17 wherein the plurality of primers consists of SEQ ID NOs: 1-12, and a set of anti-tags, the set of anti-tags having sequences complementary to nucleotides 1-24 of SEQ ID NOs: 1-12.

19. (Previously presented) A combination comprising the composition of claim 17 wherein the plurality of primers consists of the complete complements of SEQ ID NOs: 1-12, and a set of anti-tags, the set of anti-tags having sequences complementary to nucleotides 1-24 of the complete complements of SEQ ID NOs: 1-12.

20. (Previously presented) The combination of claim 18, wherein each anti-tag is attached to a spectrally coded bead specific for the anti-tag.

21. (Previously presented) The combination of claim 19, wherein each anti-tag is attached to a spectrally coded bead specific for each anti-tag.

22. (Previously presented) An improved method of simultaneously detecting in a sample the presence or absence of variant nucleotides associated with thrombosis, wherein the improvement comprises simultaneously identifying the presence or absence of variant nucleotides associated with thrombosis via allele specific primer extension using a set of primers having the sequences set forth in SEQ ID NOs: 1-12.